

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
2 September 2004 (02.09.2004)

PCT

(10) International Publication Number
WO 2004/073606 A3

(51) International Patent Classification⁷: **C07D 333/62**,
409/12, C07C 311/29, 311/16, C07D 213/71, 231/18,
213/74, 263/32, 333/34, 231/12, 277/36, 319/18, 409/04,
307/79

(21) International Application Number:
PCT/US2004/002015

(22) International Filing Date: 10 February 2004 (10.02.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/448,307 14 February 2003 (14.02.2003) US

(71) Applicant (for all designated States except US): **ELI LILLY AND COMPANY** [US/US]; Lilly Corporate Center, Indianapolis, Indiana 46285 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **CONNER, Scott**, Eugene [US/US]; 8426 Carefree Circle, Indianapolis, Indiana 46236 (US). **GOSSETT, Lynn, Stacy** [US/US]; 7345 Donegal Drive, Indianapolis, Indiana 46217 (US). **GREEN, Jonathan, Edward** [US/US]; 7464 Glendale Drive, Avon, Indiana 46123 (US). **JONES, Winton, Dennis Jr.** [US/US]; 1227 East 126th Street, Carmel, Indiana 46033 (US). **MANTLO, Nathan, Bryan** [US/US]; 7325 East County Road 800 North, Brownsburg, Indiana 46112 (US). **MATTHEWS, Donald, Paul** [US/US]; 7736 Wawasee Drive, Indianapolis, Indiana 46250 (US). **MAYHUGH, Daniel, Ray** [US/US]; 9681 Troon Court, Carmel, Indiana 46032 (US). **SMITH, Daryl, Lynn** [US/US]; 11830 Ashton Drive, Fishers, Indiana 46038 (US). **VANCE, Jennifer, Ann** [US/US]; 132 El Bosque, San Jose, California 95134 (US). **WANG, Xiaodong** [CN/US]; 14066 Honey Tree Drive, Carmel, Indiana 46032 (US). **WARSHAWSKY, Alan, M** [US/US]; 13828 Springmill Ponds Circle, Carmel, Indiana 46032 (US). **WINNEROSKI, Leonard, Larry Jr.** [US/US]; 587 Thoroughbred Lane, Greenwood, Indiana 46142 (US). **XU, Yanping** [CN/US]; 13832 Barnett Place, Fishers, Indiana 46038 (US). **ZHU, Guoxin** [CN/US]; 9972 Parkshore Drive, Noblesville, Indiana 46060 (US).

(74) Agents: **JANG, Soonhee et al.**; **ELI LILLY AND COMPANY**, P. O. Box 6288, Indianapolis, Indiana 46206-6288 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

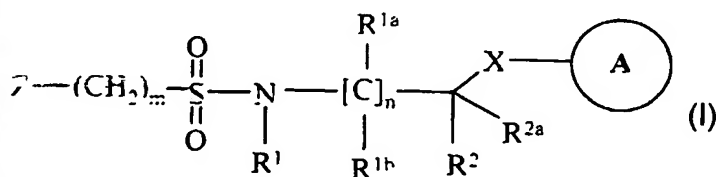
Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

— as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ,

[Continued on next page]

(54) Title: SULFONAMIDE DERIVATIVES AS PPAR MODULATORS



(57) Abstract: The present invention is directed to a compound of Formula (I), and pharmaceutically acceptable salts, solvates, hydrates or stereoisomers thereof, which are useful in treating or preventing disorders mediated by a peroxisome proliferator activated receptor (PPAR) such as syndrome X, type II diabetes, hyperglycemia, hyperlipidemia, obesity, coagulopathy, hypertension, arteriosclerosis, and other disorders related to syndrome X and cardiovascular diseases.



EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

— of inventorship (Rule 4.17(iv)) for US only

Published:

— with international search report

(88) Date of publication of the international search report:

31 March 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D333/62 C07D409/12 C07C311/29 C07C311/16 C07D213/71
 C07D231/18 C07D213/74 C07D263/32 C07D333/34 C07D231/12
 C07D277/36 C07D319/18 C07D311/13 C07D409/04 C07D307/79

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	M. SATO ET. AL.: "Synthesis and evaluation of novel fluorinated sulotroban-related sulfonamide derivatives as thromboxane A2 receptor antagonists." EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, vol. 30, 1995, pages 403-14, XP002296706 tables I-III	1-4, 7-10, 13, 14, 25
X	M. SATO ET. AL: "Asymmetric synthesis of the sulfoxide metabolite of ON-579 by the Kagan protocol." BIOORGANIC AND MEDICINAL CHEMISTRY LETTERS, vol. 7, no. 19, 1997, pages 2451-4, XP002296707 table I	1-4, 7-10, 13, 14, 25

--/--

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

21 September 2004

Date of mailing of the international search report

21/10/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Helps, I

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	K. SHINOZAKI ET. AL.: "Synthesis and thromboxane A2 antagonistic activity of indane derivatives." BIOORGANIC AND MEDICINAL CHEMISTRY LETTERS, vol. 9, 1999, pages 401-6, XP002296708 tables 1,2	1,25
X	M. SATO ET. AL: "Synthesis and evaluation of novel sulfonamide derivatives as thromboxane A2 receptor antagonists I." EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, vol. 29, 1994, pages 185-90, XP002296709 tables I,II	1-4, 7-10,13, 14,17,25
X	J. P. BERLOT ET. AL.: "Preparation of a dansylated fibrate, a new fluorescent tool to study peroxisome proliferation. Effect on hepatic-derived lines." BIOCHEMIE, vol. 79, 1997, pages 145-50, XP002296710 page 148	1-4, 7-10,13
X	K. G. LIU ET. AL.: "Identification of a Series of PPARGgamma/delta dual Agonists Via Solid-Phase Parallel Synthesis." BIOORGANIC AND MEDICINAL CHEMISTRY LETTERS, vol. 11, 2001, pages 2959-62, XP002296711 page 2960, column 1, paragraph 1 - page 2961, column 1, paragraph 1	1-4, 7-10,13, 14
X	US 6 518 290 B1 (SIERRA) 11 February 2003 (2003-02-11)	1
A	intermediate compound D, claims; examples	1-40
X	US 6 306 854 B1 (BROWN ET. AL.) 23 October 2001 (2001-10-23)	1
A	intermediate compound 14, claims; examples	1-40
A	US 6 369 098 B1 (PERSHADSINGH ET. AL.) 9 April 2002 (2002-04-09) column 1 - column 3; claims; examples	1-40
P,A	WO 03/072099 A (ELI LILLY) 4 September 2003 (2003-09-04) page 1, line 1 - page 2, line 7; claims; examples	1-40
A	EP 1 167 357 A (SANKYO) 2 January 2002 (2002-01-02) page 1, line 1 - page 2, line 20; claims; examples	1-40
	-/--	

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6 248 781 B1 (JEPPESEN ET. AL.) 19 June 2001 (2001-06-19) column 1; claims; examples -----	1-40

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/002015

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 27-39 (part)
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 27-39 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6518290	B1	11-02-2003	AT 265442 T 15-05-2004
		AU 758758 B2 27-03-2003	
		AU 2003001 A 12-06-2001	
		BR 0016067 A 06-08-2002	
		CA 2393190 A1 07-06-2001	
		DE 60010333 D1 03-06-2004	
		DK 1244642 T3 16-08-2004	
		EP 1244642 A1 02-10-2002	
		HU 0203532 A2 28-02-2003	
		JP 2003515597 T 07-05-2003	
		NO 20022467 A 26-07-2002	
		PL 356772 A1 12-07-2004	
		CN 1402716 T 12-03-2003	
		CZ 20021903 A3 15-01-2003	
		WO 0140207 A1 07-06-2001	
		TR 200201473 T2 23-09-2002	
		TW 555753 B 01-10-2003	
		ZA 200204241 A 02-07-2003	
US 6306854	B1	23-10-2001	AU 6350699 A 08-05-2000
		EP 1149063 A2 31-10-2001	
		WO 0023407 A2 27-04-2000	
		JP 2002527496 T 27-08-2002	
US 6369098	B1	09-04-2002	AU 7995300 A 10-05-2001
		WO 0125226 A1 12-04-2001	
		US 2002019344 A1 14-02-2002	
		AU 8827101 A 25-02-2002	
		WO 0213812 A1 21-02-2002	
WO 03072099	A	04-09-2003	WO 03072099 A1 04-09-2003
EP 1167357	A	02-01-2002	AU 760163 B2 08-05-2003
		AU 3670700 A 23-10-2000	
		BR 0009593 A 18-06-2002	
		CA 2369871 A1 12-10-2000	
		EP 1167357 A1 02-01-2002	
		NO 20014849 A 27-11-2001	
		NZ 514661 A 30-06-2003	
		PL 351898 A1 30-06-2003	
		US 2004002512 A1 01-01-2004	
		US 2003069294 A1 10-04-2003	
		CN 1353694 T 12-06-2002	
		CZ 20013593 A3 13-03-2002	
		HU 0200895 A2 28-11-2002	
		WO 0059889 A1 12-10-2000	
		JP 2001097955 A 10-04-2001	
		RU 2219172 C2 20-12-2003	
		TR 200102908 T2 22-04-2002	
		ZA 200108168 A 18-02-2003	
US 6248781	B1	19-06-2001	US 2001031762 A1 18-10-2001
		US 2001031764 A1 18-10-2001	
		US 2001031786 A1 18-10-2001	
		AU 6325899 A 08-05-2000	
		WO 0023417 A1 27-04-2000	
		EP 1123269 A1 16-08-2001	
		JP 2002527503 T 27-08-2002	